

A rare case of ureteral metastasis of invasive ductal breast carcinoma twenty years later

Ureteral metastasis of invasive breast cancer

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Abstract

Breast cancer is the most frequently diagnosed malignancy in women; however, ureteral metastasis, particularly five or more years after the initial diagnosis, has rarely been reported in the literature. We present a case of ureteral metastasis of invasive ductal breast carcinoma twenty years post-diagnosis in a 61-year-old female who was admitted to our hospital with abdominal pain. Abdominal ultrasonography and computerized tomography revealed a 36×27×21 mm solid mass around the left ureter. The patient underwent trucut biopsy, and after histopathologic examination and immunostaining, a diagnosis of invasive ductal breast carcinoma metastasis was determined. The patient received preoperative radiotherapy and surgical resection of the metastatic lesion has been planned. In a patient with a history of breast cancer, a thorough radiological examination of even the most unlikely secondary sites should be performed.

Keywords

Breast cancer; Metastasis; Ureter

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Introduction

Breast cancer is the most frequently diagnosed cancer in women worldwide. Approximately 12% of patients develop metastatic disease after surgery. Common metastatic sites of breast cancer include the lymph nodes, lungs, liver, and bone. Metastasis to the retroperitoneum and ureter are extremely rare [1,2]. The metastatic patterns of lobular and ductal carcinoma of the breast are different while gastrointestinal system, gynecologic organ, and peritoneum-retroperitoneum metastases markedly are more prevalent in lobular breast carcinoma [3]. Ureteral metastasis from any prior tumor is very rare, and according to the literature, prostate, bladder, breast, and gut cancer, as well as lymphoma, are the most common primary tumors [4]. Here, we report a case of ureteral metastasis twenty years after a diagnosis of invasive ductal breast carcinoma.

Case Report

A 61-year-old female patient presented with abdominal pain. Twenty years ago, she was diagnosed with left breast cancer and underwent mastectomy. Postoperative pathological examination revealed invasive ductal carcinoma. General physical examination was unremarkable with complete blood count, other routine laboratory tests, and complete urine analysis results all within normal limits. However, ultrasonography showed an enlarged left renal pelvis (grade 3 hydronephrosis). Abdominal computerized tomography confirmed the hydronephrosis as a lobular contoured mass around the left ureter, which was 36×27×21 mm in size. With a clinical diagnosis of primary or metastatic ureteral malignancy, the patient underwent trucut biopsy. Histopathological examination showed infiltration of tumor tissue (Figure 1). Architecturally, the tumor was characterized by a mix of large invasive nests, a trabecular pattern, and a small number of glandular differentiation. The tumor consisted of atypical pleomorphic cells and enlarged hyperchromatic nuclei. There was also mitotic activity and a large necrotic area. In addition, lymphovascular invasion was identified. Immunohistochemistry (IHC) revealed that the tumor was positive for GATA-binding protein 3 (GATA3), gross cystic disease fluid protein 15 (GCDFP-15) (Figure 2), estrogen receptor (ER), progesterone receptor (PR), and mammaglobin (focal), while negative for uroplakin III and p63. The expression of Ki-67, a cell proliferation marker, was high. Human epidermal growth factor receptor 2 (HER2) was 2+ and silver stain hybridization in situ (SISH) analysis of HER2 gene amplification was negative. This case consisted of a diagnosis of invasive ductal breast carcinoma metastasis supported by histopathological and immunohistochemical findings. The patient was referred to the medical oncology department where she received preoperative radiotherapy, and surgical resection of the isolated metastatic lesion is currently being planned.

Discussion

Even if fewer than 10% of breast cancers first manifest with metastasis, metastatic relapse occurs in about 50% of patients within three years of initial diagnosis [5]. Although our case is unusual as the patient was initially diagnosed with breast cancer nearly twenty years prior, there have been similar cases reported. For example, Zhou [2] reported a case with an

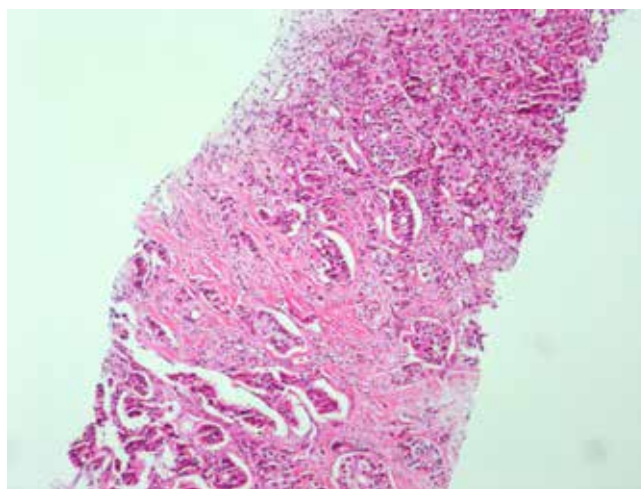


Figure 1. Histological section of the ureter infiltrated by tumor cells (HE, x100).

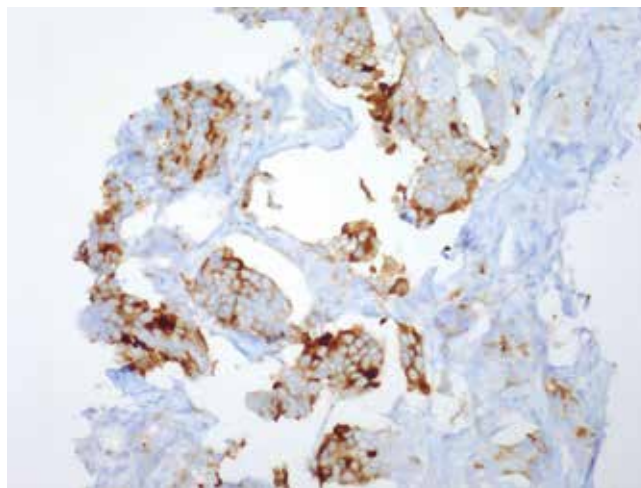


Figure 2. Tumor cells stained positively with GCDFP 15 (IHC, x200).

eight-year history of breast cancer before presenting ureteral metastasis; Mondaini [5] reported a case of ureteral metastasis from a primary breast cancer where the disease recurred with an episode of renal colic 7 years after diagnosis; and finally, Gabsi [1] reported a case of breast cancer with ureteral metastasis at the time of diagnosis.

Metastatic tumors of the ureter are uncommon because the ureters do not have a continuous longitudinal network of lymphatic and blood vessels, and are, therefore, resistant to metastasis by these two routes. According to autopsy data, the incidence of ureteral metastasis is 8.3%. The majority of ureteric metastatic cancers are asymptomatic and the incidence of diagnosing ureteral metastasis in patients while they are alive is exceedingly rare. However, increased accessibility to radiographic testing has greatly increased the rate of incidental findings [6]. Although there are cases with nonspecific symptoms – such as lumbar pain, nausea, urinary tract infection, and weight loss, pain due to ureteral obstruction is the most frequent [2]. Thus, insidious symptoms should alert clinicians to consider retroperitoneal metastases as a possible cause of unexplained back, flank, or abdominal pain in patients with a long history of breast cancer [1]. In the described case, the patient presented with abdominal pain, which was investigated by radiological imaging. Ultrasonography and computerized tomography revealed hydronephrosis, which was a secondary effect due to a new ureteral mass.

It is important, but difficult, to differentiate between primary and secondary tumors of the ureter. MacKenzie and Ratner developed criteria for actual ureteral metastasis in 1931. They noted that in metastatic growths of the ureters, malignant cells can always be seen in the perivascular lymphatic spaces or the blood vessels around the ureter. These criteria were later modified by Presman and Ehrlich as follows: demonstration of malignant cells in a portion of the ureteral wall without direct invasion. Periureteral adventitia of the ureter is generally the first layer involved because this part of the ureter is rich in blood vessels [2]. In our case, the tumor mass had grown around the ureteral wall and the tumor cells were found within the immediate periureteral lymphatics. The detection of asymmetric wall enhancement, wall thickening, and urinary obstruction are the expected imaging findings; however, from an imaging standpoint, the differentiation of ureteral metastasis from primary urothelial tumors may be difficult with the current technologies available. Histopathologic evaluation is necessary in most cases [6]. Cytologic study findings of urine are infrequently positive because metastatic ureteral tumors tend not to penetrate into the mucosa [2].

Most metastatic tumors of the urinary tract present as a single mass that can resemble a primary tumor but the histopathology can reflect the tumor origin. Immunohistochemistry or other special studies are required to differentiate between primary tumors and metastases, and to determine the origin of the latter. Architecturally, the invasive ductal breast carcinoma may be arranged in cords, clusters, or trabeculae, while others are characterized by a predominantly solid or syncytial infiltrative pattern with little associated stroma. Glandular differentiation may be obvious as tubular structures with central lumina in tumor-cell groups. Single-file infiltration or targetoid features can be seen but these lack the characteristics of invasive lobular carcinoma. The tumor cells are more pleomorphic than lobular carcinoma and they express E-cadherin. A wide range of mitotic and necrotic cells can also be seen. The stromal component may have fibroblastic proliferation or marked hyalinization. In a minority of cases, lymphoplasmacytic infiltrate can be identified. GATA3 is expressed in primary and metastatic ductal and lobular carcinomas of breast and urothelial carcinomas. Metastatic breast cancers are also evaluated for GCDFP-15 and mammaglobin. In the presence of metastatic deposits from an unknown source, immunoreactivity for GATA3, GCDFP-15, mammaglobin, and hormone receptors strongly suggest a primary breast tumor, especially when positive for all markers [7]. Urothelial carcinomas are usually positive for high molecular weight cytokeratin (34 β E12), p63, thrombomodulin, and uroplakin III. In the present case, the tumor was immunoreactive against GATA3, GCDFP-15, mammaglobin, ER, PR, while negative for p63 and uroplakin III strongly suggests a primary breast tumor. Several studies have demonstrated discordance in up to 40% for hormone receptors and up to 20% for HER2 status between primary tumors and metastatic diseases [3]. Discordant hormone receptor and HER2 status between the primary tumor and metastatic site play an important role in clinical decision-making for patient treatment.

The survival decreases greatly in patients with distant metastases. The overall 5-year relative survival rate is 99% for

localized diseases and drops to 27% for distant metastases [8]. Currently, there is no cure for ureteral metastasis of breast cancer, and treatment depends on the intrinsic characteristics of the tumor and clinical features of the patient. Ureteral catheterization is recommended in patients with ureteral obstruction. To allow for this procedure, surgical resection of isolated metastatic lesions may be required and to improve symptomatology. However, when ureteral catheterization is not possible, nephrostomy or ureteric reimplantation may be necessary. Radiotherapy may be used to target the tumor or postsurgical tumor site. However, most patients with metastasis of the ureter have metastatic lesions elsewhere and systemic therapy is generally required, the most common of which is chemotherapy. Alternatives of chemotherapy include hormonal therapy, molecular-targeted therapy, immunotherapy, and more recently, nanotechnology and gene therapy [1,2]. In our case, the patient is alive and has received preoperative radiotherapy. Surgery is currently being planned.

In conclusion, the main cause of mortality among breast cancer patients is the metastatic spread of the primary tumor. The nonspecific symptoms of metastasis add to the difficulties of making the diagnosis. Although rare, if there is a history of breast carcinoma, a patient with abdominal pain should be suspected of ureteral metastasis due to breast carcinoma even if it appears several years later [1,2,5].

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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